

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | | |
|--|---|---|------------------|
| Applicant's or agent's file reference SCB/PB60730 | FOR FURTHER ACTION | | See item 4 below |
| International application No. PCT/GB2005/000350 | International filing date (day/month/year) 01 February 2005 (01.02.2005) | Priority date (day/month/year) 03 February 2004 (03.02.2004) | |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | | |
| Applicant GLAXO GROUP LIMITED | | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

| | |
|---|---|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70 | Date of issuance of this report 07 August 2006 (07.08.2006) |
| | Authorized officer Nora Lindner e-mail: pt02@wipo.int |

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 12 MAY 2005

11 Aug 05

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2005/000350

International filing date (day/month/year)
01.02.2005

Priority date (day/month/year)
03.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D407/H2, C07D213/B2, C07D409/H2, A61K31/4433, A61K31/4418, A61K31/4436, A61P25/04

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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D-80298 Munich
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Fax: +49 89 2399 - 4465

Authorized Officer

Usuelli, A

Telephone No. +49 89 2399-7366



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000350

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000350

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 9-10 (industrial applicability)

because:

- ☒ the said international application, or the said claims Nos. 9,10 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000350

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-10 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-10 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-8 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 9 and 10 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims, cf. Article 34(4)(a)(i) PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1- Reference is made to the following documents:

D1: WO 02/062750 A (SCHERING CORPORATION) 15 August 2002 (2002-08-15)

2- Novelty

D1 does not disclose any pyridine derivative having the same substitution pattern of present compounds of formula (I).

Accordingly, the requirements of Art.33.2 PCT are met.

3- Inventive step

3.1- The applicant has set himself the task of providing novel agents capable to modulate the cannabinoid receptor in particular the sub receptor CB2.

Document d1 relate to polycyclic compounds having the same use of present compounds. Taking into account of the data disclosed on page 19 of the application, it appears credible that substantially all the claimed compound modulate the CB2 receptor.

Accordingly, the objective technical problem can be seen in the provision of further CB2 modulators.

3.2- The skilled person faced with the technical problem defined above would not find any hint in d1 for preparing present compounds of formula (I).

Accordingly, the requirements of Art. 33.3 PCT are met.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000350

Re Item VI

Certain documents cited

- D2: WO 2004/029026 A (GLAXO GROUP LIMITED; EATHERTON, ANDREW, JOHN;
GIBLIN, GERARD, MARTIN,) 8 April 2004 (2004-04-08)
- D3: WO 2004/029027 A (GLAXO GROUP LIMITED; EATHERTON, ANDREW, JOHN;
GIBLIN, GERARD, MARTIN,) 8 April 2004 (2004-04-08)

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INTERNATIONAL SEARCHING AUTHORITY

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Date of mailing
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Applicant's or agent's file reference
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FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2005/000350

International filing date (day/month/year)
01.02.2005

Priority date (day/month/year)
03.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D407/H2, C07D213/B2, C07D409/H2, A61K31/4433, A61K31/4418, A61K31/4436, A61P25/04

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

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- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
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For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Authorized Officer

Uselli, A

Telephone No. +49 89 2399-7366



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000350

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
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2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
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☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000350

Box No. III Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability

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- ☐ the entire international application,
- ☒ claims Nos. 9-10 (industrial applicability)

because:

- ☒ the said international application, or the said claims Nos. 9,10 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
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 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000350

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-10 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-10 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-8 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 9 and 10 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims, cf. Article 34(4)(a)(i) PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1- Reference is made to the following documents:

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3- Inventive step

3.1- The applicant has set himself the task of providing novel agents capable to modulate the cannabinoid receptor in particular the sub receptor CB2.

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Accordingly, the objective technical problem can be seen in the provision of further CB2 modulators.

3.2- The skilled person faced with the technical problem defined above would not find any hint in d1 for preparing present compounds of formula (I).

Accordingly, the requirements of Art. 33.3 PCT are met.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000350

Re Item VI

Certain documents cited

- D2: WO 2004/029026 A (GLAXO GROUP LIMITED; EATHERTON, ANDREW, JOHN;
GIBLIN, GERARD, MARTIN,) 8 April 2004 (2004-04-08)
- D3: WO 2004/029027 A (GLAXO GROUP LIMITED; EATHERTON, ANDREW, JOHN;
GIBLIN, GERARD, MARTIN,) 8 April 2004 (2004-04-08)